PB83-231266

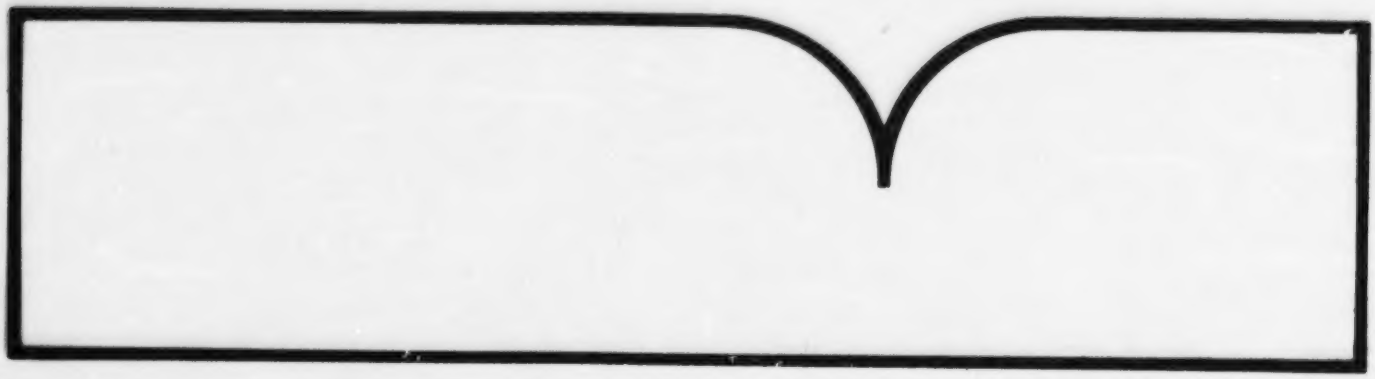
Selenium Levels in Human Blood, Urine, and Hair in Response to Exposure via Drinking Water

California Univ., Los Angeles

Prepared for

Health Effects Research Lab.
Research Triangle Park, NC

1978



U.S. Department of Commerce
National Technical Information Service
NTIS

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before comple

1. REPORT NO.	2.	3 PB83-231266
EPA-600/J-78-198		

4. TITLE AND SUBTITLE	5. REPORT DATE
Selenium Levels in human Blood, Urine, and Hair in Response to Exposure via Drinking Water (Journal Version)	1978
	6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO
Valentine, Jane L., Kang, Han K., Spivey, Gary H.	
9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
School of Public Health, Center for Health Sciences University of California Los Angeles, California 90024	CBMCIA
	11. CONTRACT/GRANT NO.
	R-803798-1
12. SPONSORING AGENCY NAME AND ADDRESS	13. TYPE OF REPORT AND PERIOD COVERED
Health Effects Research Laboratory U.S. Environmental Protection Agency Research Triangle Park, NC 27711	14. SPONSORING AGENCY CODE EPA-600/11

15. SUPPLEMENTARY NOTES
Citation: Valentine, Jane L., Kang, Han K., Spivey, Gary H., Selenium Levels in Human Blood, Urine and Hair In Response to Exposure via Drinking Water, Envr. Rsch., 17, 347-355 (1978)

16. ABSTRACT

(Project Officer: Daniel Greathouse)

Blood, hair, urine and tap water samples were obtained from participants in a population exposed to varying amounts of selenium via water from home wells. Concentrations of selenium in urine and hair produced significant positive correlations with well-water selenium levels. Blood selenium with well-water selenium did not produce a significant correlation. Urine selenium correlation with hair selenium and urine selenium correlation with blood selenium were found to be significant. No significant correlation for hair selenium with blood selenium was found. We conclude that blood selenium alone is not an adequate monitor of selenium exposure or body burden at levels below chronic toxicity.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS (This Report)	21. NO. OF PAGES
Release to Public	unclassified	10
	20. SECURITY CLASS (This page)	22. PRICE
	unclassified	

EPA Form 2220-1 (Rev. 4-77) PREVIOUS EDITION IS OBSOLETE

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

EPA-600/J-78-198
JOURNAL ARTICLE

ENVIRONMENTAL RESEARCH 17, 347–355 (1978)

Selenium Levels in Human Blood, Urine, and Hair in Response to Exposure via Drinking Water

JANE L. VALENTINE, HAN K. KANG, AND GARY H. SPIVEY

School of Public Health, Center for Health Sciences, University of California, Los Angeles, California 90024

Received February 22, 1978

Blood, hair, urine, and tap water samples were obtained from participants in a population exposed to varying amounts of selenium via water from home wells. Concentrations of selenium in urine and hair produced significant positive correlations with well-water selenium levels. Blood selenium with well-water selenium did not produce a significant correlation. Urine selenium correlation with hair selenium and urine selenium correlation with blood selenium were found to be significant. No significant correlation for hair selenium with blood selenium was found. We conclude that blood selenium alone is not an adequate monitor of selenium exposure or body burden at levels below chronic toxicity.

INTRODUCTION

Selenium, an essential element to some animal species, is controversial in its association with health status in man. It has been linked to the human diseases of cancer (Schrauzer and Rhead, 1971; Shamberger and Willis, 1971; Sharpiro, 1972; Shamberger *et al.*, 1973; McConnell *et al.*, 1975; Broghamer *et al.*, 1976), muscular distrophy (Walton, 1962), infant death (Money, 1970; 1971; Rhead *et al.*, 1972; Saltzstein *et al.*, 1973; Cowgill, 1976), dental caries (Cadwell and Cousins, 1960; Hadjimarkos, 1960, 1965; Hadjimarkos and Bonhorst, 1961), and teratogenicity (Robertson, 1970). Most of the above reports used body fluids to assess selenium status but no consistent choice of fluids or tissues (e.g., blood and urine or blood and hair) was made. In addition, most of the studies cited made no determination of the individuals' sources of exposure or of the individuals' variations in selenium status, accumulation, or excretion, in response to those sources of exposure.

In assessing the selenium–disease relationship, blood and urine seem to be the most common fluids examined; levels in hair or nails are rarely measured. This rare use of hair and nails as a monitor is surprising in view of their usefulness in assessing the body burden of other trace elements (Hammer *et al.*, 1972). Since there are many body tissues and fluids that could be used as monitors of selenium status, it is important to determine which one or which combination would be best or most appropriate.

This paper is a report of our findings for selenium concentrations in whole blood, urine, and hair, with a complete set of tissues being obtained from each individual in a population exposed to various amounts of selenium via local drinking water. Such data allowed us to assess the relationship between exposure levels of selenium in the tissues and fluids, and to determine which best reflect body burden.

0013-9351/78/0173-0347$02.00/0

MATERIALS AND METHODS

A study population consisting of forty-three residents from a small community in Milan, New Mexico was chosen. This community was selected as a result of prior data received from the New Mexico Environmental Improvement Agency dating from 1975 showing that the home wells in that area contained amounts of selenium ranging from 10 to as much as 3900 μg/liter. In comparison, the United States drinking water standard is 10 μg/liter. Presumably each home well had become contaminated due to a uranium mill tailing pond nearby.

Sample collection was conducted over a 4-day period. Scalp hair, blood, a 24-hr urine specimen, and a sample of tap water were obtained from each participant. However, all samples, i.e., hair and urine, could not be obtained from each person which explains variability in sample sizes. A questionnaire was administered to determine dietary habits, occupational history, and length of residence. No participant was included in the study unless he had used his present water supply for at least 1 year.

Sample preparation consisted of thorough washing of the entire hair samples with nonionic detergent, ethyl alcohol, and distilled, deionized water rinse. The total amount of hair was taken since each participant had to have lived in the community at least 1 year in order to be included in the study. Thus a steady state with respect to intake and excretion of selenium was assumed. Hair samples so prepared and whole blood, urine, and water samples were wet ashed with nitric and perchloric acids. Analysis was done according to a modified method (Kang and Valentine, 1977) which uses 6 $\times$ HCl instead of a 20% HCl solution to dilute the digests. The procedure employs a hydride-generating sampling system using sodium borohydride for gas generation with subsequent analysis of generated hydrogen selenide by atomic absorption spectrophotometry.

Duplicate samples of trace metal reference standard prepared by U.S. EPA were analyzed in each measurement along with other biological samples. In all cases accuracy was within $\pm$ 5% of the EPA value. When known amounts of selenium were added to distilled, deionized water and carried through the entire procedure (acid digestion, hydride generation), recoveries of added selenium were within $\pm$ 10% of added amounts.

Statistical correlations were determined by linear regression analysis.

RESULTS

The population surveyed was uniform in terms of its exposure to possible selenium from food, air, and occupational sources. Questionnaire results did not reveal any significant or varying consumption of possible selenium-containing foods (i.e., fish, grains, animal meats) by participants. Since the study group came from the same geographical location, and due to the presumption that the selenium contamination was a result of a uranium mill tailing pond it was assumed that selenium intake via food would be similar for all participants. No occupational exposure to selenium was revealed. The average length of residence for the population was 9.5 years. Such a long-length residence further supported our steady state assumption applied to hair samples.

The range and average concentrations of selenium in water, whole blood, urine, and hair are given in Table 1, along with the average concentrations for the same

TABLE 1

SELENIUM CONCENTRATIONS IN HUMAN BLOOD, URINE, HAIR, AND WATER SAMPLES

Sample	Present study			Reported in literature			
	No. of samples	Mean ± SD	Range	No. of samples	Mean ± SD	Range	Reference
Blood (μg/100 ml)	43	17.1 ± 2.4	13.3–24.8	250	18.0 ± 3.7	Not given	Dickson and Tomlinson (1967)
				48	22.9 ± 3.5	Not given	Shamburger *et al.* (1973)
				210	20.6[a]	10.0–34.0	Allaway *et al.* (1968)
				10	21.7 ± 1.1	17.0–27.3	Shamberger and Willis (1971)
Urine (μg/liter)	35	79.3 ± 38.7	21.5–203.0	793	34 ± 24	0–150	Glover (1967)
				15	42 ± 18	0–69	Sterner and Lindfeldt (1941)
Hair (μg/g)	39	0.46 ± 0.40	0.02–2.0	8	0.57 ± 0.04	0.36–0.74	Schroeder *et al.* (1970)
Water (μg/liter)	19	537 ± 650	26–1800				

[a] No SD given.

biological specimens as reported by others. The mean concentration for urine selenium was greater than the mean values previously reported. The mean hair selenium concentration was similar to that reported by Schroeder *et al.* (1970). However, our range of selenium demonstrated a wide spread reflecting the wide range of selenium intake via water. Schroeder *et al.*'s average value is a result of only eight samples showing a small spread in values reported. Our values for blood are within the normal limits reported. Only 7% of the blood selenium concentrations was above 20 μg/100 ml.

Linear regression analysis on arithmetic selenium concentrations for urine and hair against well-water selenium produced statistically significant correlations of 0.54 and 0.58, respectively, at the $P < 0.01$ level. The correlation coefficient, 0.13, obtained for the arithmetic selenium concentrations in blood against well-water selenium concentrations was not statistically significant ($P > 0.05$).

The regression analysis assumes that the variance of y (selenium concentration in biological sample) is constant for all values of x (water selenium concentration). However, the scatter of the points for the arithmetic plots (not reported) suggested that a logarithmic transformation would better satisfy this assumption. Thus the log–log plot for body burden versus water concentration was performed. Such plots of urine selenium against well-water selenium and hair selenium against well-water selenium are shown in Figs. 1 and 2. Correlation coefficients of 0.57 and 0.45 for the respective tissues were found to be statistically significant at the $P < 0.01$ level. The correlation coefficient obtained for blood selenium concentrations versus concentrations in water was not found to be significant, $r = 0.14$ at $P > 0.05$ (Fig. 3). Correlation coefficients and corresponding level of significance remained the same with or without the logarithmic transformation.

Correlations of selenium concentrations between different combinations of tissues produced positive and statistically significant correlations for urine with hair ($r = 0.65$, $P < 0.001$) and for urine with blood ($r = 0.40$, $P < 0.05$). The respective

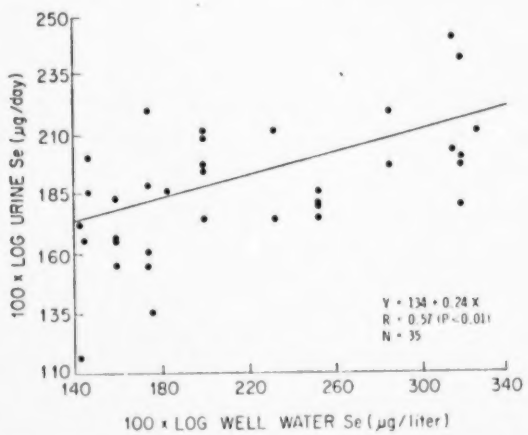


FIG. 1. Individual urinary selenium concentration plotted as a function of selenium concentration in well water.

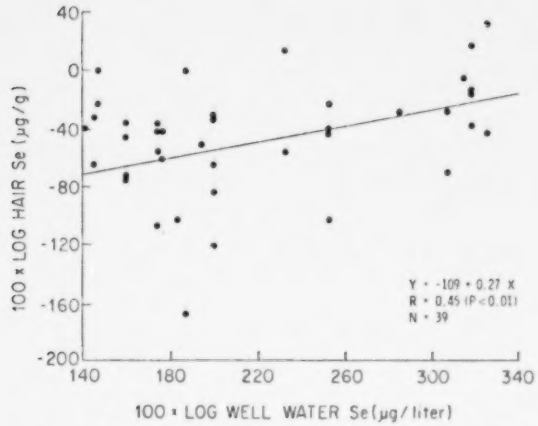


FIG. 2. Individual hair selenium concentration plotted as a function of selenium concentration in well water.

graphs are shown in Figs. 4 and 5. For the urine–hair plot (Fig. 4) one extreme point seemed to affect the correlation coefficient obtained. However when this point was eliminated a correlation coefficient of 0.41 was obtained which was still statistically significant ($P < 0.05$). Since blood selenium concentrations did not correlate significantly with well-water concentration while the other tissues did, it is surprising to find a significant correlation between blood and urine. However, without the two extreme points in Fig. 5 for the plot of urine selenium with blood selenium, the correlation coefficient becomes 0.21 which is not statistically significant ($P > 0.05$). The relationship between hair and blood, shown in Fig. 6 was not found to be significant ($r = 0.28$, $P > 0.05$).

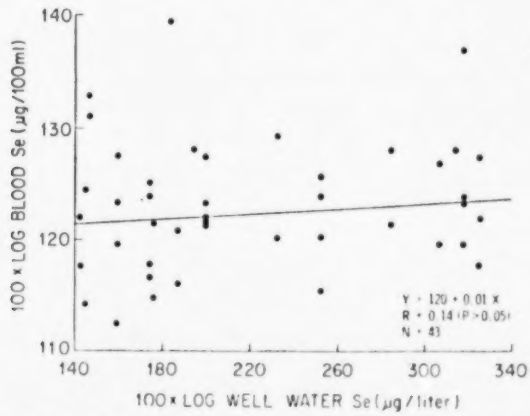


FIG. 3. Individual blood selenium concentration plotted as a function of selenium concentration in well water.

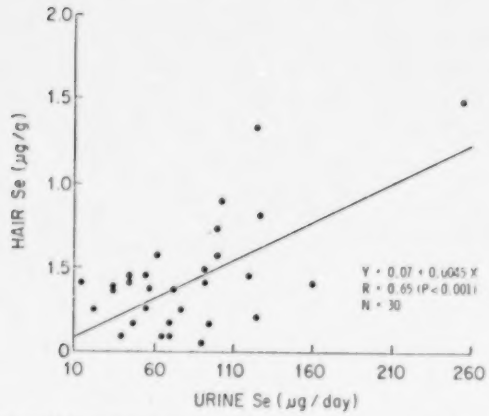


FIG. 4. Individual hair selenium concentration plotted against concentration of selenium in urine.

DISCUSSION AND CONCLUSIONS

Blood selenium levels are often used in assessing selenium status. But, animal experiments (Burk *et al.*, 1968; Scott and Thompson, 1971) suggest that the blood selenium level does not continue to rise with increases in dietary selenium once adequate selenium intake is achieved. If toxic selenium intake is reached then increases in intake are again reflected in increases in blood selenium levels. Human blood selenium concentrations seem to follow a similar pattern and seem to be regulated at the approximate concentration of 20 μg/100 ml (Burk, 1976). It is possible that a homeostatic mechanism existed in those individuals surveyed in our present study. Thus our finding of only 7% of the blood selenium concentrations being greater than 20 μg/100 ml would not be unexpected even with the relatively high levels of selenium intake via the drinking water. If such a regulatory mechanism exists, no correlation between water selenium and blood selenium would be anticipated.

Urinary excretion in rats seems to reflect dietary intake of selenium (Burk,

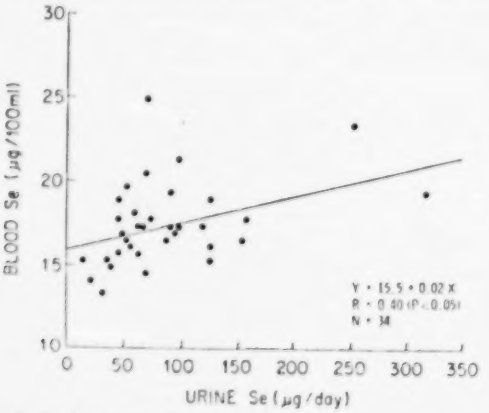


FIG. 5. Individual blood selenium concentration plotted against concentration of selenium in urine.

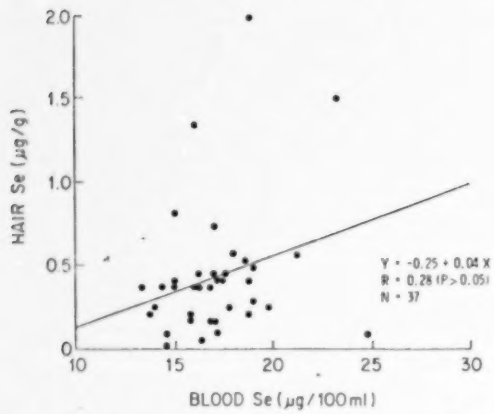


FIG. 6. Individual hair selenium concentration plotted against concentration of selenium in blood.

1976). Burk and co-workers (1972) showed that the amount of ^{75}Se appearing in the urine was related to the level of selenium in the diet fed to rats. They postulated the existence of a threshold dietary level of selenium between 0.054 and 0.074 ppm. Smith and co-workers (1938) also observed that urinary excretion of selenium is directly related to dietary intake. When rats were poisoned with sodium selenite, 50 to 80% was eliminated by the urine and only 20% or less by the feces. The good correlation we obtained for urine selenium with water selenium seems to reflect these findings.

Westfall and Smith (1940) suggested the use of hair as an index of the extent of chronic selenium poisoning. They correlated the degree of selenium exposure from food with the resulting amounts of selenium found in the hair, liver, kidney, blood, and urine of rabbits and cats. Hair selenium levels were shown to increase with selenium exposure. Correlations of human hair selenium levels to selenium exposure have not been previously reported. Our data suggest that hair would serve as a useful monitor of selenium exposure.

The nonsignificance of the correlations of blood selenium with water selenium and of blood selenium with hair selenium is of importance since blood is used quite often to assess the degree of exposure and to assess the selenium–disease relationship in humans (Schrauzer and Rhead, 1971; Shamberger and Willis, 1971; Shamberger *et al.*, 1973; McConnell *et al.*, 1975; Broghamer *et al.*, 1976). Our findings suggest that in such assessments it is not sufficient to use only blood as an indication of selenium status. Urine selenium comparisons with hair selenium and with water selenium gave significant positive correlations and suggest that urine or hair measurements would be more likely to give valid results. Thus if blood is to be used, another biological specimen, e.g., hair or urine, should be monitored simultaneously.

ACKNOWLEDGMENTS

This investigation was supported by Research Grant R-803798-01 from the U.S. Environmental Protection Agency. We are grateful for the assistance provided by Ms. Mai Dang for selenium analysis and Mr. Mark Schluchter for statistical analysis.

REFERENCES

Allaway, W. H., Kubota, J., Losee, F., and Roth, M. (1968). Selenium, molybdenum, and vanadium in human blood. *Arch. Environ. Health* **16**, 342–348.

Broghamer, W. L., McConnell, K. P., and Blotcky, A. L. (1976). Relationship between serum selenium levels and patients with carcinoma. *Cancer* **37**, 1384–1388.

Burk, R. F. (1976). Selenium in man. *In* "Trace Elements in Human Health and Disease. Essential and Toxic Elements" (A. S. Prasad and D. Oberleas, Eds.), Vol. 2. Academic Press, New York.

Burk, R. F., Brown, D. G., Seely, R. J., and Scaief, C. C. (1972). Influence of dietary and injected selenium on whole-body retention, route of excretion, and tissue retention of $^{75}SeO_3^{2-}$ in the rat. *J. Nutr.* **102**, 1049–1055.

Burk, R. F., Whitney, R., Frank, H., and Pearson, W. N. (1968). Tissue selenium levels during the development of dietary liver necrosis in rats fed torula yeast diets. *J. Nutr.* **95**, 420–428.

Cadwell, P. B., and Cousins, F. B. (1960). Urinary selenium and dental caries. *Nature (London)* **185**, 863–864.

Cowgill, U. M. (1976). Selenium and neonatal death. *Lancet* **1**, 816.

Dickson, R. C., and Tomlinson, R. H. (1967). Selenium in blood and human tissues. *Clin. Chim. Acta* **16**, 311–321.

Glover, J. R. (1967). Selenium in human urine: A tentative maximum allowable concentration for industrial and rural population. *Ann. Occup. Hyg.* **10**, 3–14.

Hammer, D. I., Finklea, J. F., Hendricks, R. H., Hinners, T. A., Riggan, W. B., and Shy, C. M. (1972). Trace metals in human hair as a simple monitor of environmental exposure. *In* "Trace Substances in Environmental Health-V. A Symposium." Univ. of Missouri Press, Columbia.

Hadjimarkos, D. M. (1960). Urinary selenium and dental caries. *Nature (London)* **4751**, 677.

Hadjimarkos, D. M. (1965). Effect of selenium on dental caries. *Arch. Environ. Health* **10**, 893–899.

Hadjimarkos, D. M., and Bonhorst, C. W. (1961). The selenium content of eggs, milk and water in relation to dental caries in children. *J. Pediat.* **59**, 256–259.

Kang, H. K., and Valentine, J. L. (1977). Acid interference in the determination of arsenic by atomic absorption spectrophotometry. *Anal. Chem.* **49**, 1829–1832.

McConnell, K. P., Broghamer, W. L., Blotcky, A. J., and Hurt, O. J. (1975). Selenium levels in human blood and tissues in health and disease. *J. Nutr.* **105**, 1026–1031.

Money, D. F. L. (1970). Vitamin E and selenium deficiencies and their possible aetiological role in sudden death in infants syndrome. *N.Z. Med. J.* **71**, 32–33.

Money, D. F. L. (1971). Cot deaths and deficiency of vitamin E and selenium. *Brit. Med. J.* **4**, 559.

Rhead, W. J., Saltzstein, S. L., and Cary, E. E. (1972). Vitamin E, selenium and the sudden infant death syndrome. *Clin. Notes Respir. Dis.* **81**, 415–416.

Robertson, D. S. F. (1970). Selenium—a possible teratogen. *Lancet* **1**, 518–519.

Saltzstein, S. L., Schrauzer, S. N., and Rhead, W. J. (1973). Sudden infant deaths and deficiencies in diet. *J. Amer. Med. Ass.* **226**, 466.

Schrauzer, G. N., and Rhead, W. J. (1971). Interpretation of the methylene blue reduction test of human plasma and the possible cancer protecting effect of selenium. *Experientia* **27**, 1069–1071.

Schroeder, H. A., Frost, D. V., and Balassa, J. J. (1970). Essential trace metals in man: selenium. *J. Chronic Dis.* **23**, 227–243.

Scott, M. L., and Thompson, J. N. (1971). Selenium content of feedstuffs and effects of dietary selenium levels upon tissue selenium in chicks and poults. *Poultry Sci.* **50**, 1742–1748.

Shamberger, R. J., Rukovena, E., Longfield, A. K., Tytko, S. A., Deadbar, S., and Willis, C. E. (1973). Antioxidants and cancer: I, Selenium in the blood of normal and cancer patients. *J. Nat. Cancer Inst.* **50**, 863–870.

Shamberger, R. J., and Willis, C. E. (1971). Selenium distribution and human cancer mortality. *CRC Crit. Rev. Clin. Lab. Sci.* **2**, 211–221.

Sharpiro, J. R. (1972). Selenium and carcinogenesis: A review. *Ann. N.Y. Acad. Sci.* **199**, 215–226.

Smith, M. I., Westfall, B. B., and Stohlman, E. F. (1938). Studies on the fate of selenium in the organism. *Pub. Health Rep.* **53**, 1199–1216.

Sterner, J. H., and Lidfeldt, V. (1941). The selenium content of "normal" urine. *J. Pharmacol. Exp. Ther.* **73**, 205–211.

Walton, J. N. (1962). Selenium and vitamin E in nutrition. Muscular dystrophy in man: Clinical aspects. *Proc. Nutr. Soc.* **21**, 202–205.

Westfall, B. B., and Smith, M. I. (1940). Chronic selenium: IV, Selenium in the hair as an index of the extent of its deposition in the tissues in chronic poisoning. *Nat. Inst. Health Bull.* **174**, 45–49.